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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,137	02/15/2002	Browning Jeffrey	A080 US	2907

65779 7590 06/14/2007

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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/077,137	JEFFREY ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20,25-27,29,32,33,35,36,38-40,42,43,45-47,49,50 and 52-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20,25-27,29,32,33,35,36,38-40,42,43,45-47,49,50 and 52-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment and response filed 3-28-07 has been entered into the record. Claims 19, 20, 25-27, 29, 32-33, 35, 36, 38-40, 42, 43, 45-47, 49, 50 and 52-61 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

The rejection of claim 25 under 35 U.S.C. 102(a) as anticipated by Gross et al (WO/00/40716, published 13 July 2000) is withdrawn.

Rejections Maintained

Priority

Applicants again argue the assignment of priority. It is clear from the statute that Applicants are only entitled to priority when they comply with 35 USC 112, first paragraph having written description and enablement of the later claimed invention. The claims are drawn to pharmaceutical compositions. Applicants argue that the examiner has not established a prima facie burden taht 60/149,378 does not enable the claimed invention. This is not persuasive; the Office provided a plethora of evidence and reasoning. Applicants argue that the art provided by the examiner indicates that the immune system can be manipulated by administration of single molecules. This is not persuasive because extensive *in vivo* experimentation was needed to demonstrate such activity. The molecule described by Applicant is novel to the art and therefore cannot rely upon activities of different molecules to establish in vivo therapeutic efficacy. In contrast to the instant case, those of the art the roles of the ligand in the diseases process was well established. The Office has established that B cell maturation and differentiation can be controlled by different cytokines in an apparently overlapping or redundant manner. It is not clear that

by manipulating one cytokine that one could affect B cell proliferation, maturation or immunoglobulin production. The record establishes that the interplay of cytokines in B cell maturation/proliferation and immunoglobulin production is complex. Applicants seek to establish that the Office burden rises to the unreasonable level that must provide explicit data to indicate that the invention does not work. It is maintained that the Office has provided reasons to doubt the asserted truth of the statements of the 1999 provisional document. Applicants argue that the art followed the teachings of the provisional document to produce Applicants invention (Huntington et al, 2006). It is unclear how Applicants reach this conclusion as Huntington et al does not appear to cite Applicants provisional application at issue herein. The 1999 document provides no *in vitro* data providing for a nexus to *in vivo* efficacy and therefore no reasonable expectation of success that the claimed pharmaceutical compositions could be so used. The 1999 priority document does not provide *in vitro* data demonstrating the activities of inhibiting B-cell growth or immunoglobulin production or both. There is no nexus because no *in vitro* activity is described that would provide for reasonable expectation of the *in vivo* activity as instantly claimed. It was not until the later priority documents does Applicants provide the requisite activity assays. Applicants reiterate the language of the priority document indicated that because they say 95% identical, they were in possession of these variants. This is also not persuasive; no sequence variants were described. A single sequence was described 1-51 Ig fusion to bind BAFF (SEQ ID NO:9). No binding fragments (8-41) or 95% variants were described. The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it (i.e. by screening for binding to SEQ I DNO:9). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmacentical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian

FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Furthermore, the courts have held that the presence of a screening assay to detect the desired compound is not a description of the compound itself. Therefore, while the provisional document may have described 1-51, 1-52, and 8-41, it does not describe variants of these sequences. *University of Rochester v. G.D. Searle & Co,* 58 F.3d 916, 69 USPQ 1886 (Fed. Cir. 2004). Applicants have not provided a description of a representative number of variants to demonstrate possession of the genus because these are new and unknown polypeptides. No evidence of efficacy or binding of the peptide 8-41 of SEQ ID NO:1 to SEQ ID NO:9 has been provided in any of the provisional documents. The skilled artisan would have to use independent judgment, to develop specific assays, determine if the composition worked *in vitro* and then make the leap to *in vivo* studies to ascertain if the claimed peptides were able to have any effect at all the complex milieu of cytokines *in vivo*. Such independent thought, discovery and judgment goes beyond the skill in the art and is the act of invention. The experimentation is not routine, the physiological process *in vivo* complex and therapeutic efficacy unpredictable. The experimentation is not routine experimentation it is the essence of discovery. It is undue to actually have to discover if the composition works *in vitro* and then discover if the composition works *in vivo*. *Enzo Biochem Inc. v. Calgene Inc.* 52 USPQ2d 1129 (CAFC 1999). "A recurring problem is whether a specification that sets forth a single or a limited number of examples can be enabling of broad claims when the subject matter concerns biological materials or reactions which are generally considered to be unpredictable." (Page 1138) In the instant case, there are no examples of *in vitro* efficacy for the functions set forth in the claims in the 1999 document and no description of variants thereof in any later document. There is no reasonable nexus provided because no demonstration of *in vitro* activity of affecting B cell growth or immunoglobulin production provided in the provisional document and therefore no reasonable expectation of success *in vivo* based on similar TNF receptors in

the art as argued by Applicants. As such, it is maintained that Applicants are not entitled to priority to the 1999 provisional document because this document is not enabled for the claimed invention. Applicants argue the USPTO written description guidelines. This is not persuasive, these are guidelines only and each case is decided on its own merits. Applicants argue that there is no requirement that the experimentation be predictable or the outcome 100% predictable and cites *In re Wands* and *In re Angstadt*. *Wands* and *Agnstadt* provided a working embodiment of the invention and the courts concluded that it was not undue experimentation to screen for others because the experimentation was routine. This is completely in contrast to the instant case because the priority document does not provide an *in vitro* data demonstrating the requisite activity of any specie that falls within the genus. How can one routinely screen for others, when the 1-51-Ig fusion was not demonstrated to have the ability to inhibit B cell growth or immunoglobulin production *in vitro*? The instant fact scenario is completely different than *Wands* or *Angstadt* for which Applicants attempt to rely. Furthermore, in contrast to Applicants arguments the unpredictability in the art is a consideration in the enablement of the priority document and the specification. In reaching a conclusion of undue experimentation, the following factors have been considered: *quantity of experimentation necessary, amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, relative skill of those in the art, the predictability or unpredictability of the art* and the breadth of the claims (*In re Wands* (CAFC) 8 USPQ2d 1400). Applicants argue that variants could be discovered by mere routine effort. This again is not persuasive because the 8-41 fragments has not been demonstrated to have any *in vitro* activity how can one screen for variants thereof. Additionally, the specification has not described any variants and cannot rely upon a known or disclosed correlation of structure with function because the structure is not known to the art (i.e. described in the specification as new or novel) and the specification does not teach a representative number of changes that would have activity. The Office maintains

that in applications directed to inventions in arts but where the results are unpredictable (pharmaceutical compositions), the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. The claims are not limited to the post-filing evidence for practicing the invention. As such, priority to the 1999 document is denied to the variants or to 8-41 fragment and variants thereof.

Claims 19, 20, 25-27, 29, 32-33, 35, 36, 38-40, 42, 43, 45-47, 49, 50 and 52-60 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising an isolated B cell activating factor receptor (BAFF-R) of SEQ ID NO: 1 or a fragment comprising residues 1-51 of SEQ ID NO: 1 that binds B cell activating factor (BAFF), wherein the BAFF-R is optionally fused to the Fc region of an immunoglobulin it does not reasonably provide enablement for sequence variants, naturally occurring variants, allelic variants, mammalian homologues or percent variants thereof and fusions to an immunoglobulin per se. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons made of record in the all the prior Office Actions and herein.

Applicant's arguments were addressed under priority issues above.

The rejection of claims 19, 20, 26, 27, 29, 32, 33, 36, 38-40, 43, 45-47, 50 and 52-60 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gross et al (WO/00/40716, published 13 July 2000) is maintained for reasons made of record in the Office Action mailed 3-17-05.

Applicants' arguments have been carefully considered but are not fully persuasive. Applicants argue that they are entitled to the priority date of provisional application 60/149,378 filed August 17, 1999. This is not persuasive, the provisional document lacks written description and is not enabled for reasons made of record above and is not enabled for the claimed invention reasons made of record herein.

However, it is noted that the provisional document 60/181,684 and 60/183,356 are enabled for pharmaceutical compositions comprising the 1-51 and 1-52 fragments of SEQ ID NO:1 in view of the activity profiles presented therein, but not enabled for 8-41 or 95% variants for reasons made of record herein.

Claims 19, 20, 26, 27, 29, 32, 33, 36, 38-40, 43, 45-47, 50 and 52-60 stand rejected under 35 U.S.C. 102(e) as anticipated by Shu et al (U.S. Patent No. 6,475,987, issued November 5, 2000, filed May 5, 2000 with benefit of priority to May 1, 2000, provisional application 60/201,012).

Applicants' arguments have been carefully considered but are not fully persuasive. Applicants argue that they are entitled to the priority date of provisional application 60/149,378 filed August 17, 1999. This is not persuasive, the provisional document lacks written description and is not enabled for reasons made of record above and is not enabled for the claimed invention reasons made of record herein. Applicants also argue that the provisional document of Shu et al does not provide description of the relied upon subject material. This is not persuasive the provisional document does in fact discuss the receptors for TALL-1. TALL-1 is the same molecule as BAFF and therefore the prior art discloses a BAFF receptor by another name.

However, it is noted that the provisional document 60/181,684 and 60/183,356 are enabled for pharmaceutical compositions comprising the 1-51 and 1-52 fragments of SEQ ID NO:1 in view of the activity profiles presented therein, but not enabled for 8-41 or 95% variants for reasons made of record herein.

Claims 19, 20, 26, 27, 29, 32, 33, 36, 38-40, 43, 45-47, 50 and 52-60 are rejected under 35 U.S.C. 102(e) as anticipated by Shu et al (U.S. Patent Application Publication 2003/0148445 A1, published August 7, 2003, with benefit of priority to May 1, 2000, provisional application 60/201,012).

Applicants' arguments have been carefully considered but are not fully persuasive. Applicants argue that they are entitled to the priority date of provisional application 60/149,378 filed August 17, 1999. This is not persuasive, the provisional document lacks written description and is not enabled for reasons made of record above and is not enabled for the claimed invention reasons made of record herein. Applicants also argue that the provisional document of Shu et al does not provide description of the relied upon subject material. This is not persuasive the provisional document does in fact discuss the receptors for TALL-1. TALL-1 is the same molecule as BAFF and therefore the prior art discloses a BAFF receptor by another name.

However, it is noted that the provisional document 60/181,684 and 60/183,356 are enabled for pharmaceutical compositions comprising the 1-51 and 1-52 fragments of SEQ ID NO:1 in view of the activity profiles presented therein, but not enabled for 8-41 or 95% claimed variants for reasons made of record.

Allowable Subject Material

Claims limited to residues 1-51 or 1-52 of SEQ ID NO:1 are allowable over the prior art of record.

Status of Claims

All claims stand rejected.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to

reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Jeffrey Siew can be reached on 571-272-0787.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy

Primary Examiner

Art Unit 1645